Applicant: George L. King Serial No.: 10/027,204

Filed: December 21, 2001

Page: 5

In the claims:

Please amend the claims as follows:

DRAFT

DETERMINING

Claim 1. (Currently Amended) A method of evaluating approtein kinase C (PKC) activity in a cardiovascular tissue other than monocytes of a subject, the method comprising:

be real and the evaluating the level of the PKC activity in monocytes of the subject,

the level of PKC activity in the monocytes being correlated to the level of PKC activity in the <u>cardiovascular</u> tissue ether than monocytes.

Claim 2. (Original) The method of claim 1, wherein the PKC activity is PKC  $\beta$  activity.

Claim 3. (Canceled)

Claim 4. (Currently Amended) The method of claim 3 1, wherein the cardiovascular tissue is retinal, kidney or aorta vascular tissue or heart.

Claim 5. (Original) The method of claim 1, wherein the subject is a human.

Claim 6. (Original) The method of claim 1, wherein the subject is an experimental animal.

Claims 7-15. (Canceled)

Claim 16. (Currently Amended) A method of evaluating a subject for the extent, stage, or severity, of a PKC related disorder cardiovascular complication of diabetes, the method comprising:

evaluating the level of PKC activity in monocytes of the subject; and optionally comparing the level of the PKC activity in monocytes of the subject with a standard,

Applicant: George L. King Serial No.: 10/027,204

Filed: December 21, 2001

Page : 6

the level of PKC activity being correlated with the extent, stage, or severity, of the PKC related disorder cardiovascular complication of diabetes.

Claim 17. (Currently Amended) The method of claim 16, wherein the <u>diabetic</u> complication is <u>diabetic retinopathy</u> disorder is <u>diabetes</u>.

Claim 18. (Currently Amended) The method of claim 16, wherein the <u>diabetic</u> complication is <u>diabetic</u> nephropathy <u>disorder</u> is a cardiovascular disorder.

Claim 19. (Currently Amended) The method of claim 16, wherein the <u>diabetic</u> complication is <u>disorder</u> is <u>diabetes mellitus</u>, <u>Type I diabetes</u>, <u>Type II diabetes</u>, <u>diabetic</u> retinopathy, <u>proliferative diabetic retinopathy</u>, <u>non proliferative diabetic retinopathy</u>, <u>diabetic nephropathy</u>, <u>microalbumiuria</u>, <u>proteinuria</u>, <u>renal failure</u>, hypertension, atherosclerosis, coronary artery spasm, congestive heart failure, coronary artery disease, valvular disease, arrhythmias, and cardiomyopathy.

- Claim 20. (Original) The method of claim 16, wherein the PKC activity is PKC  $\beta$  activity.
  - Claim 21. (Original) The method of claim 16, wherein the subject is a human.
- Claim 22. (Original) The method of claim 16, wherein the subject is an experimental animal.

EFFICACY OF

Claim 23. (Currently Amended) A method of evaluating the effect of a treatment for a PKC related disorder cardiovascular complication of diabetes on a subject comprising:

administering a treatment for a <u>cardiovascular complication of diabetes</u> PKC related disorder to a subject; and

evaluating the level of a PKC activity in monocytes of the subject, thereby evaluating the effect of the treatment.



Applicant: Ge rge L. King Serial No.: 10/027,204

Filed: December 21, 2001

Page: 7

Attorney's Docket No.: 10276-066001

Claim 24. (Currently Amended) The method of claim 23, wherein the disorder is diabetes complication is diabetic retinopathy.

Claim 25. (Currently Amended) The method of claim 23, wherein the disorder is a eardiovascular disorder complication is diabetic nephropathy.

Claim 26. (Currently Amended) The method of claim 23, wherein the disorder is diabetes mellitus, Type I diabetes, Type II diabetes, diabetic retinopathy, proliferative diabetic retinopathy, proliferative diabetic

Applicant: George L. King Serial No.: 10/027,204

Filed: December 21, 2001

Page: 7

Claim 24. (Currently Amended) The method of claim 23, wherein the disorder is diabetes complication is diabetic retinopathy.

- Claim 25. (Currently Amended) The method of claim 23, wherein the disorder is a cardiovascular disorder complication is diabetic nephropathy.
- Claim 26. (Currently Amended) The method of claim 23, wherein the disorder is diabetes mellitus, Type I diabetes, Type II diabetes, diabetic retinopathy, proliferative diabetic retinopathy, non-proliferative diabetic retinopathy, diabetic nephropathy, microalbumiuria, preteinuria, renal failure, hypertension, atherosclerosis, coronary artery spasm, congestive heart failure, coronary artery disease, valvular disease, arrhythmias, or cardiomyopathy.
- Claim 27. (Original) The method of claim 23, wherein the PKC activity is PKC  $\beta$  activity.
  - Claim 28. (Original) The method of claim 23, wherein the subject is a human.
- Claim 29. (Original) The method of claim 23, wherein the subject is an experimental animal.
- Claim 30. (Currently Amended) A method of identifying a compound for the treatment of a PKC related disorder cardiovascular complication of diabetes in a subject, the method comprising:

administering a test compound for the treatment of the disorder complication to the subject; and

evaluating a PKC activity in monocytes of the subject, and
the level of PKC activity being correlated with the effect of the treatment on the disorder
selecting a compound if it reduces the monocyte PKC activity in the subject,
thereby identifying a compound.

DRAFT

Applicant: George L. King Serial N.: 10/027,204

Filed : December 21, 2001

Page : 8

Claim 31. (Currently Amended) The method of claim 30, wherein the disorder is diabetes complication is diabetic retinopathy.

- Claim 32. (Currently Amended) The method of claim 30, wherein the disorder is diabetes complication is diabetic nephropathy.
- Claim 33. (Currently Amended) The method of claim 30, wherein the complication is PKC related disorder is diabetes mellitus, Type I diabetes, Type II diabetes, diabetic retinopathy, proliferative diabetic retinopathy, non-proliferative diabetic retinopathy, diabetic nephropathy, microalbumiuria, proteinuria, renal failure, hypertension, atherosclerosis, coronary artery spasm, congestive heart failure, coronary artery disease, valvular disease, arrhythmias, or cardiomyopathy.
- Claim 34. (Original) The method of claim 30, wherein the PKC activity is PKC  $\beta$  activity.
- Claim 35. (Currently Amended) The method of claim 30, further comprising: optionally identifying a subject in need of a treatment for the disorder complication;
- comparing the PKC activity before the administration of the test compound to the PKC activity after administration of the test compound.

wherein a compound for the treatment of the disorder complication is identified when the PKC activity after the administration of the compound is altered compared to a standard the PKC activity before the administration.

Claim 36. (Original) The method of claim 30, wherein the subject is a human.



Applicant: George L. King Serial No.: 10/027,204

Filed : December 21, 2001

Page

(Original) The method of claim 30, wherein the subject is an experimental Claim 37. animal.

RESTRICT (Currently Amended) A method of identifying a compound for the Claim 38. treatment of aging or an aging related disorder in a subject, the method comprising:

administering a test compound for the treatment of aging or an aging related disorder to the subject; and

evaluating a PKC activity in monocytes of the subject, and the level of PKC activity being correlated with the effect of the treatment on the disorder selecting a compound if it increases the monocyte PKC activity in the subject. thereby identifying a compound for the treatment of aging.

(Currently Amended) A method of evaluating the effect of a treatment for Claim 39. aging of an aging related disorder on a subject comprising:

administering a treatment for aging or an aging related disorder to a subject; and evaluating the level of a PKC activity in monocytes of the subject, thereby evaluating the effect of the treatment.

RESTRET

- (New) A method of evaluating the relative age of a subject, the method Claim 40. comprising evaluating the level of a PKC activity in monocytes of the subject, the level of PKC activity being inversely correlated to the relative age of the subject.
- Claim 41. (New) The method of claim 40, wherein the PKC activity is PKC β activity.
  - Claim 42. (New) The method of claim 40, wherein the subject is a human.
- (New) The method of claim 40, wherein the subject is an experimental Claim 43. animal.

